

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of the Director

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## Justification

### Office of the Director

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Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.  
Reauthorizing legislation will be submitted.

Budget Authority:

FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate		Increase or Decrease	
<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>	<u>FTEs</u>	<u>BA</u>
601	\$253,463,000	605	\$273,952,000	595	\$317,983,000	-10	\$44,031,000

This document provides justification for the Fiscal Year 2004 activities of the Office of the Director (OD), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2004 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)".

## INTRODUCTION

The OD provides leadership, coordination, and guidance in the formulation of policy and procedures related to biomedical research and research training programs. To provide this direction, the OD centrally coordinates NIH's extramural and intramural research activities; science policy and related social, ethical, and legal issues; technology transfer and intellectual property protection policies; health information dissemination and education functions; legislative activities; and oversight of the agency's stewardship of public funds.

The OD encourages and fosters NIH research and research training efforts in the prevention and treatment of disease through program coordination offices that complement the efforts of the NIH Institutes and Centers (ICs). These offices focus on Acquired Immune Deficiency Syndrome (AIDS); women's health; disease prevention; science education; dietary supplements; rare diseases and disorders; and behavioral and social sciences research. While the OD provides the overall direction, coordination and oversight of these programs, the ICs manage the actual research operations.

The OD also provides direction and develops policy guidance for several administrative areas including grant and contract administration, budget and financial management, human resource

management, equal employment opportunity functions, logistics, accountable property management, and management assessment and review activities.

The FY 2004 budget request for the OD is \$317.983 million, an increase of \$44.031 million over the FY 2003 level. The specific budget requests for the various NIH-wide coordination offices and programs are presented below.

## **The Office of AIDS Research**

### **Introduction**

The NIH Office of AIDS Research (OAR), coordinates the scientific, budgetary, legislative, and policy elements of the NIH AIDS research program and serves as the principal liaison with HHS, other federal agencies, and domestic and international governmental and non-governmental organizations on behalf of NIH AIDS-related research. The NIH represents the largest and most significant public investment in AIDS research in the world. Our response to the epidemic requires a unique and complex multi-institute, multi-disciplinary, global research program. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of the NIH Institutes and Centers. This diverse research portfolio demands an unprecedented level of scientific coordination and management of research funds to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively and efficiently. This is recognized in the unique role given the OAR in its authorizing legislation, the NIH Revitalization Act of 1993. That law establishes OAR as a model for trans-NIH coordination, vesting it with primary responsibility for overseeing all NIH AIDS-related research, and thus allowing NIH to pursue a united research front against the global AIDS epidemic.

**Comprehensive AIDS Research Plan and Budget:** Each year, OAR oversees the development of the comprehensive NIH AIDS-related research plan and budget, based on scientific consensus about the most compelling scientific priorities and opportunities that will lead to better therapies and prevention strategies for HIV disease. The planning process is inclusive and collaborative, involving the NIH institutes through a series of trans-NIH Coordinating Committees, as well as eminent non-government experts from academia, foundations, and industry, with the full participation of AIDS community representatives. Historically, the Plan has established the NIH AIDS research agenda in the following Scientific Areas of Emphasis: Natural History and Epidemiology; Etiology and Pathogenesis; Therapeutics; Vaccines; and Behavioral and Social Science. As the epidemic evolved, OAR recognized the need to bring additional focus to a number of cross-cutting areas. The Plan now also includes: Racial and Ethnic Minorities; Women and Girls; Microbicides; HIV Prevention Research; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination.

The Plan is a critical document, as it serves as the framework for developing the annual AIDS research budget for each Institute and Center; for determining the use of AIDS-designated dollars; and for tracking and monitoring those expenditures. The law provides that the OAR

shall allocate all appropriated AIDS research funds to the Institutes. This process allows the OAR to ensure that NIH AIDS-related research funds will be provided to the most compelling scientific opportunities, rather than distributed simply by a formula.

**Trans-NIH Coordination:** During the course of the year, OAR identifies scientific areas that require focused attention and facilitates multi-institute activities to address those priorities. OAR fosters these efforts by designating the bulk of its resources to jump-start program areas by providing funds and supplements to the Institutes and Centers; establishing working groups or committees; sponsoring workshops or conferences to highlight a particular research topic; and sponsoring reviews or evaluations of research program areas. For example, a number of years ago OAR identified microbicides research as an area needing additional attention. OAR established a Trans-NIH Microbicides Working Group, comprised of program staff of relevant institutes and offices; co-sponsored the first international conference on microbicides; spearheaded the development of an NIH Strategic Plan for Microbicides and a broader government-wide plan; and provided supplemental funds to the institutes to accelerate microbicide research. OAR also has placed high priority on research to address the disproportionate impact of the epidemic on racial and ethnic minority communities in the U.S. by directing increased resources toward: 1) new and innovative interventions that will have the greatest impact on these groups and 2) efforts to improve research infrastructure and training opportunities for minorities.

**International AIDS Research:** OAR coordinates, monitors and fosters plans for NIH involvement in international AIDS research and training activities. OAR established a new initiative and strategic plan for global research on HIV/AIDS aimed at significantly expanding our efforts to benefit resource- and infrastructure-poor nations. OAR has designated funds for the Institutes to expand clinical research internationally, including in the areas of microbicide development, identifying therapeutic approaches appropriate for international settings, vaccine research, and research capacity building.

**Other OAR Activities:** OAR supports Coordinating Committees for each research discipline of AIDS research. These committees allow OAR to stay abreast of the scientific programs across the NIH, to foster collaboration and coordination, and to develop the annual NIH plan and budget. OAR administers an emergency discretionary fund, and the Committee has provided a transfer authority that permits OAR to move up to a total of 3% of AIDS research funds between institutes. OAR supports the Intramural AIDS Targeted Antiviral Program and the NIH AIDS Research Loan Repayment Program. OAR also supports a number of initiatives to enhance dissemination of research findings to researchers, physicians, institutions, communities, constituency groups, and patients, particularly in minority communities.

The FY 2004 budget request for the OAR is \$60.942 million. The OAR budget justification for NIH AIDS research appears under a separate tab in this Congressional Justification.

## **The Office of Research on Women's Health**

### **Introduction**

The Office of Research on Women's Health (ORWH) serves as the focal point for women's health research at NIH, with the authority and responsibility to act on behalf of the NIH Director to monitor and coordinate the activities of the NIH ICs regarding research on women's health. The Director of ORWH: (a) advises the NIH Director and staff on matters relating to research on women's health; (b) strengthens and enhances research related to diseases, disorders, and conditions that affect women; (c) ensures that research conducted and supported by NIH adequately addresses issues regarding women's health; (d) ensures that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH; (e) develops opportunities for and supports recruitment, retention, re-entry, and advancement of women in biomedical careers; and (f) supports research on women's health issues. The ORWH establishes a research agenda for women's health research, sets associated programmatic priorities, and also encourages, develops, and supports programs and opportunities for the recruitment, retention, advancement, and re-entry of women in biomedical careers. The ORWH collaborates closely with NIH ICs and the scientific and advocacy community to continually update and implement the comprehensive NIH research agenda on women's health, and to provide funding and/or cofunding through the ICs for scientifically meritorious research on women's health. In addition, the ORWH has an active outreach program, including a well-received seminar series for the NIH and neighboring scientific and lay communities.

The FY 2004 budget request for the ORWH is \$41.231 million, an increase of \$.808 million above the FY 2003 level.

### Science Advances

*Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health (SCORs):* ORWH funded a new program to foster interdisciplinary research on sex and gender factors in health. Funding for the 11 new Centers totaled \$11.8 million, of which \$9.2 was contributed by ORWH. This program, which carries a five-year commitment, also receives cofunding by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), the National Institute of Environmental Health Sciences (NIEHS), and the Food and Drug Administration (FDA). These Centers provide new opportunities for interdisciplinary approaches to advancing studies on how sex and gender factors affect women's health by promoting interdisciplinary collaborations and develop a research agenda bridging basic and clinical research on sex/gender factors underlying a priority health issue.

The research scope of the SCORs stems from three sources: the Institute of Medicine (IOM) report, "Exploring the Biological Contributions to Health Does Sex Matter?", "An Agenda for Research on Women's Health for the 21<sup>st</sup> Century," and from recommendations from the NIH ICs. Topical research themes of the new SCORs include: Pharmacology of anti-epileptic and psychotropic medications during pregnancy and lactation; Role of sex and gender differences in substance abuse relapse; Genes, androgens

and intrauterine environment in polycystic ovarian syndrome (PCOS); Sex and gender factors in the pathophysiology of irritable bowel syndrome (IBS) and interstitial cystitis (IC); Mechanisms underlying female urinary incontinence; Gender differences in pain sensitivity; Birth, muscle injury and pelvic floor dysfunction; Genetic and environmental origins of adverse pregnancy outcomes; Mechanisms by which drug transporters alter maternal and fetal drug exposure during pregnancy; Molecular and epidemiologic basis of acute and recurrent urinary tract infections (UTI's) in women; and Sex, stress and cocaine addiction.

***Chronic Fatigue Syndrome:*** Chronic Fatigue Syndrome (CFS) is a debilitating and complex syndrome that may involve multiple bodily systems and is characterized by profound fatigue, which is not alleviated by bed rest, and can be exacerbated by physical or mental activity. Persons with CFS often function at substantially lower levels of activity from their pre-onset capacities. Neither a specific cause, diagnostic test, nor treatment has been identified for this illness. It is possible that multiple subcategories of conditions are subsumed under this rubric. Approximately one percent of the total US population is affected. Caucasian women suffer with this condition more frequently than do men or women from other ethnic groups; however, epidemiologic studies conducted on inner city populations suggest that these gaps may be narrowing. Important also is that approximately 80% of people identified in such studies have not been diagnosed or treated. In addition, there is a substantial pediatric population included in the whole.

The ORWH assumed responsibility for coordinating CFS research efforts through the Trans-NIH Working Group on Chronic Fatigue Syndrome Research (CFSWG) in FY 2001. In FY 2002, ORWH spearheaded the preparation of a new program announcement to stimulate and broaden the scope of CFS research ( <http://grants.nih.gov/grants/guide/pa-files/PA-02-034.html> ). In FY2003, the website was expanded to include more scientific materials for researchers, and ORWH continues to work with other governmental and non governmental agencies to foster CFS research programs. Examples include invited participation in the CDC-sponsored meeting, *Toward Understanding the Cellular and Molecular Mechanisms of Medically Unexplained Fatigue*, in February 2003; the scientific merit review and selection of research proposals received for funding by The Chronic Fatigue Immune Dysfunction (CFIDS) Association of America; and the evaluation of the NIAMS extramural portfolio of Fibromyalgia (FM) research initiatives. The ORWH, through the CFSWG, held a scientific workshop on the interface between the brain and immune systems: *Basic Mechanisms in Chronic Fatigue Syndrome: Neuro-Immune Mechanisms*. ORWH and the CFSWG will initiate an interdisciplinary RFA based on the recommendations from this workshop. Proposals submitted in response to this RFA will be expected to address research in the context of both sex and gender differences and ethnic disparities. This initiative is designed to increase scientific knowledge about CFS and other similar multisystemic illnesses.

### New Initiatives

***Interdisciplinary Specialized Centers of Research (SCOR) on the Biology of Sex and Gender Differences (RFA):*** The ORWH, in conjunction with the NIH ICs and other DHHS agencies such as the FDA and the Agency for Healthcare Research Quality (AHRQ), will utilize budgetary increases to expand the first SCOR by reissuing the RFA in FY 04. The new RFA will emphasize current research priorities not addressed in response to the first RFA. These efforts will provide sex/gender analyses of basic and clinical biological factors that contribute to the differences between men and women in health status and health outcomes. These Centers could also explore the unique pharmacokinetics and pharmacodynamics of medications in women throughout the life cycle and including pregnancy. Special areas of research focus that may be addressed by such Centers include:

- A. Interdisciplinary Approaches to Chronic Multi-systemic Diseases with Multifactorial Etiology
- B. Sex/Gender Differences in Response to Therapeutic Interventions
- C. Care-giving and Health-related Quality of Life Issues
- D. Kidney and Urologic Health
- E. Neurobiology, including the examination of sex and endocrine differences in manifestations of brain health and of brain disorders
- F. Complementary and Alternative Medicines and Dietary Supplements
- G. Specific Organ Systems for which sex and gender studies are needed.

***Building Interdisciplinary Research Careers in Women's Health (BIRCWH) RFA:*** The ORWH seeks to reissue the institutional career development award for a third time with collaborating ICs and other DHHS agencies for the "Building Interdisciplinary Research Careers in Women's Health (BIRCWH III) Career Development Programs" to increase the number of these interdisciplinary career development awards. This third solicitation will focus specifically on institutions that address populations that experience health disparities, and/or have the potential to increase underrepresented scientists into research careers, and awards will seek to include areas of research not included in previous rounds of awards. The RFA will support research career development of junior faculty members, known as Interdisciplinary Women's Health Research (IWHR) Scholars, who have recently completed clinical training or postdoctoral fellowships, and who are commencing basic, translational, clinical and/or health services research relevant to women's health. This initiative will also promote the performance of research and transfer of findings into clinical practice that will benefit the health of women.

The BIRCWH III Programs will bridge advanced training for junior or young investigators with research independence, as well as bridge scientific disciplines or areas of interest. This will increase the number and skills of investigators at awardee institutions through a mentored research experience leading to an independent scientific career addressing women's health. This RFA uses the NIH Mentored Research Scientist Development Program Award (K12) mechanism. Awards from this RFA provide clinical, health or life sciences, or public health departments, centers, and institutes an opportunity to build national capacity for junior investigators in women's health research, here defined as including research on sex and/or gender differences, as well as research on factors that contribute to disparities in health status or health outcomes for different populations of

women. Projects may be basic, translational, clinical, or health services research, but must be within the biomedical and behavioral purview of NIH and/or the health services research purview of the AHRQ.

***Initiative on the Prevention of Chronic Diseases in Girls and Women:*** Chronic diseases are the leading cause of death and disability for women in the United States. Recent data indicate that many of these diseases have their beginnings during childhood, adolescence and young adulthood. There is convincing evidence that preventive actions during this period can have beneficial effects on reducing the incidence, morbidity and mortality for a number of chronic diseases that affect women across their life span.

In terms of a working definition, chronic diseases can be defined as those conditions that require ongoing medical attention and health care, in most instances also requiring long-term medication use. Within that definition would fall conditions such as Diabetes, Autoimmune disorders, cardiovascular disease, musculo-skeletal disorders, and other degenerative disorders such as Alzheimer's Disease.

One of the most important areas for the prevention of chronic diseases in girls and women across the life span is physical activity. Recent national reports indicate the rising prevalence of obesity in adolescents due to poor eating habits and irregular physical activity. Weight concerns also are related to an adolescent girl's risk of initiating cigarette smoking. Recent reports confirm the marked decline in physical activity in both African-American and Caucasian girls. All of these factors lead to increased morbidity and mortality as a woman ages. Therefore, these factors as they contribute to excess mortality from chronic diseases will be the focus of this research initiative.

***Health Disparities of and among Women:*** For certain diseases, such as HIV/AIDS and other sexually transmitted diseases, autoimmune diseases, cancer, cardiovascular diseases, and diabetes, the burden of morbidity and mortality falls disproportionately on certain populations of girls and women. These groups have been traditionally underrepresented in research, such as those from diverse cultures, members of minority groups, the elderly, and those dwelling in rural or inner city communities. Lack of information about how specific diseases affect members of diverse groups differently also contributes to the health care community's inability to provide optimum care for many Americans.

A special focus on health-promoting behaviors and other factors that contribute to these health disparities, including the translation of research findings to these communities, will be addressed through this initiative.

***Benign Uro-Gynecological Conditions:*** A research initiative will focus on benign urogynecologic, such as pelvic floor disorders, urinary incontinence, uterine fibroids, and endometriosis. ORWH, in collaboration with appropriate ICs, will expand research to address the pathophysiology of these conditions as well as innovative and successful alternative

interventions. In addition, recent scientific advances increasing the understanding of childbirth-related and neuro-muscular injuries, provide basic, clinical and translational research opportunities in this general area.

## **The Office of Behavioral and Social Sciences Research**

### **Introduction**

The Office of Behavioral and Social Sciences Research (OBSSR) furthers the mission of NIH by emphasizing the role that behavioral and social factors and their interaction with biomedical variables play in health. The three main goals of the Office are to 1) enhance behavioral and social sciences research and training; 2) integrate a biobehavioral perspective across NIH; and 3) improve communication among health scientists and with the public. Specifically, the major responsibilities of the Office include the following:

- o providing leadership and direction to increase the scope of and support for behavioral and social sciences research and training at the NIH;
- o advising key NIH officials on matters relating to behavioral and social sciences research;
- o serving as the principal spokesperson on the importance of behavioral and social sciences research in the acquisition, treatment, and prevention of disease and disability;
- o stimulating research in the behavioral and social sciences and interdisciplinary research;
- o providing leadership in disseminating findings from behavioral and social sciences research;
- o and sponsoring seminars, workshops, and conferences at the NIH and at national and international scientific meetings on behavioral and social sciences research.

Since its establishment in 1995, the Office has made significant progress in fulfilling each of its goals, including organizing 16 trans-NIH funding activities, sponsoring seven major conferences and cosponsoring multiple workshops and trans-NIH planning groups. The budget request for OBSSR in FY 2004 is \$26.179 million.

### **Science Advances**

***Interaction of Genes and Environments.*** In-depth understanding of pathways to disease and preservation of good health necessitates the study of the joint effects of genes and environments. For example, recent research has revealed that specific genes can be expressed at different points in an organism's life. Whether a particular gene is expressed, and the degree to which it is expressed, depend strongly on the environmental conditions experienced by the organism. Such gene expression is implicated in both positive and negative health effects. In October 2001, OBSSR joined with the National Human Genome Research Institute (NHGRI) to hold a planning meeting bringing together leading geneticists and social/behavioral scientists to discuss ways to facilitate the development of this field of research. During the remainder of FY

**2002, OBSSR and NHGRI worked together to establish a Trans-NIH Committee on the Interaction of Genes and Environments. The**

**committee is exploring avenues for cooperation and coordination amongst NIH Institutes and Centers (ICs) and is developing a series of workshops, conferences, and lectures toward the ultimate goal of joint funding initiatives.**

***Social and Cultural Factors in Health.* In FY 2002, OBSSR in collaboration with 15 NIH ICs issued a program announcement (PA) calling for increased research on the influence of social and cultural factors on health and illness. The program announcement is the direct result of the OBSSR-sponsored conference on "Higher Levels of Analysis" and represents continuing efforts to achieve a better understanding of the interdependence of social, behavioral, and biological levels of analysis in health research. Topics addressed included sociocultural constructs such as race, ethnicity, socioeconomic status, and gender; sociocultural linkages between demographic factors and health; social and cultural factors in prevention, treatment, and health services; interpersonal, neighborhood, and community influences on health; health justice and ethical issues; and global perspectives on health.**

***Exploring the Behavioral and Biological Pathways Between Education and Health.* While the positive association between education and health has been well-documented, there is a paucity of scientific information on the biological mechanisms and the causal pathways which underpin this association. In October 2002, OBSSR cosponsored a workshop on Education Pathways to Health with the Princeton Center for Health and Well-being. The workshop recommended several areas for further research which will be pursued in a Request for Applications (RFA) to be funded in FY 2003. Several ICs will contribute funds to the RFA either in FY 2003 or 2004.**

***Integrating Behavioral Medicine into the Medical School Curriculum.* In FY 2002, OBSSR funded a project with the Institute of Medicine (IOM). This project had several goals. The first is to review the approaches used by medical schools that have successfully incorporated behavioral and social sciences into their curricula and the second is to develop a list of prioritized topics from the behavioral and social sciences for possible inclusion in medical school curricula. The project will also examine the barriers to integrating behavioral medicine into medical school curricula. The next generation of physicians and biomedical scientists must have an increased knowledge of behavioral and social science because they are fundamental to understanding disease etiology and to promoting health. Approximately half of all causes of mortality in the US are linked to social and behavioral factors such as smoking, diet, alcohol use, sedentary lifestyle, and accidents. The IOM report will be issued in FY 2004 and possibly followed by an RFA or PA in FY 2004 or FY 2005.**

***Methodological Workshops to Advance the Behavioral and Social Sciences.* Increasingly, the community or neighborhood is viewed as a contributing factor to the health and well-being of its members. However, research to identify the aspects of the community that affect health has been hampered by the need to develop new and improved ways of**

measuring communities and their various characteristics. An OBSSR sponsored working group of scientists conducting community research identified ways by which OBSSR could facilitate

community research initiatives to improve research methods and measure in the area. Based on recommendations from the workshop, collaborative activities among OBSSR and several NIH ICs are under development.

***Economic Perspectives on Health Disparities.*** OBSSR and the National Center on Minority Health and Health Disparities sponsored research to expand the understanding of the economic implications of racial and ethnic health disparities in the US, specifically to examine the potential economic benefit to society of research and resulting interventions that would eliminate disparities, to estimate the health care system costs associated with health disparities, to estimate the effects of health disparities on labor market performance, and to explore the evidence relating disparities in health to investments in education. The results of this research were presented at a symposium in December 2001. Several of the research papers presented are currently under review and are expected to be published jointly.

***Ethical Issues in Behavioral and Social Sciences Research.*** Given the importance of behavioral and social sciences in the federal research enterprise, the new DHHS Office of Human Research Protections has requested that OBSSR assist in reviewing the distinctive and common issues for biomedical and behavioral/social sciences research. In addition, OBSSR has spearheaded the reissue of an Ethics PA that supports research regarding ethics topics within various institutes at NIH. The PA addresses crosscutting issues involving, but not limited to, informed consent, risk and benefits, and selection of subjects.

***Methodology and Measurement in the Behavioral and Social Sciences.*** Recognizing the importance of providing support for the development of the tools for research, in FY 2002, OBSSR led a trans-NIH activity to develop and issue a PA in methodology and measurement in the behavioral and social sciences. This PA was issued in March 2002. Research was sought in areas such as the processes that underlie self reports, research design, data collection techniques, measurement, data analysis techniques, and related ethical issues.

***Racial/Ethnic Bias and Health.*** The high rates of disparities in health outcomes among various racial and ethnic groups in the US call for a careful examination of the factors contributing to those differences. Racial and ethnic bias, both within the health care system and society at large, has been identified as a contributor. In an effort to further understand the role of racial/ethnic bias in health disparities, OBSSR convened a meeting of leading scientists to present scientific evidence of the effects of racial and ethnic bias on health and to identify areas for future research to further explicate the relationship. A research agenda for understanding how racial bias may impact on health and how the effects might be ameliorated was developed. The recommendations from these activities will be used to provide guidance for trans-NIH program activities to fund research on racial bias and health.

## **New Activities**

***Evaluating Internet Interventions.*** Consumers, patients, and providers are increasingly using e-health applications, particularly the Internet, to seek health information. These technologies offer people the ability to obtain and appropriately utilize health information at relatively low cost, including those with limited or no access to health care professionals or services, and historically underserved populations. Although numerous health websites are available and some e-health applications look promising, more rigorous evaluation is needed on the quality and the effects of those designed specifically for health behavior change and chronic disease management. Research is also needed on provider behavior in adopting and utilizing these technologies with their patients. A 2003 initiative, sponsored by The Robert Wood Johnson Foundation (RWJF), is a small scale grant-making program that supports pilot research to evaluate the effectiveness of e-health applications for health behavior change and chronic disease management. OBSSR proposes to hold a 2004 trans-NIH planning meeting to coordinate a follow-up RFA for larger scale evaluations, building on RWJF's pilot work.

***Maintenance of Long Term Behavioral Change.*** Mounting evidence suggests the need for research that examines biopsychosocial processes and tests interventions designed to achieve long-term health behavior change. Research efforts funded by a recent OBSSR-coordinated RFA were successful in achieving behavioral change during and immediately following the intervention phase. However, other research indicates that relapse rates for addictive behaviors such as substance abuse and tobacco use are very high. For example, most individuals who stop smoking cigarettes relapse within six months. Adherence to exercise, diet and other health regimens is no better, despite the fact that initial success rates for various behavior change programs are very good. Thus long-term behavior change is as challenging, if not more so, than the initiation of behavior change. Past research efforts have typically focused on short term behavioral change. In FY 2004, OBSSR will implement an initiative that will encourage investigators to expand on the current theoretical base of change processes and intervention models, to expand our understanding of how change, once achieved, is maintained over the long term.

**Training for Conducting Behavioral Randomized Clinical Trials.** The relevance of behavioral and social processes and interventions to health research has become increasingly clear over the past three decades. Research findings are now at the level where evaluation of interventions through Randomized Clinical Trials (RCTs) is becoming more and more necessary. However, behavioral RCTs present unique challenges (e.g., the identification and implementation a proper "placebo" or control group), and few behavioral scientists have training or experience in conducting RCTs. In consultation with experts, OBSSR developed and fully financed a 12-day-long Summer Training Institute for Randomized Clinical Trials Involving Behavioral Interventions, which it held in 2001 and 2002. Each year more than 400 scientists have expressed interest in the course, and more than 180 submitted applications for the 30

fellowships. The participants rated the training experience as "excellent." With the goal of creating a cadre of behavioral and biomedical scientists trained in evaluating behavioral interventions, OBSSR intends to continue supporting the Summer Training Institutes for five more years. In addition, OBSSR has organized a series of symposia to provide similar training to NIH staff starting in FY 2003.

**Expanding the Initiative on Mind-Body Interactions and Health.** The Public Health Service has documented that many of the leading causes of morbidity and mortality in the US are attributable to social, behavioral, and lifestyle factors (e.g., tobacco use, lack of exercise, poor diet, and alcohol abuse). Numerous studies have also documented that psychological stress is linked to a variety of health outcomes, and researchers and public health officials are becoming increasingly interested in understanding the nature of this relationship. Research has shown, for example, that psychological stress can contribute to increased heart disease and decreased immune system functioning. In 1999, using funds especially appropriated by Congress to the OBSSR, the NIH issued an RFA for Centers for Mind-Body Interactions and Health (OD-99-005) and subsequently awarded five P50 Center Grants ([http://obssr.od.nih.gov/RFA\\_PAs/MindBody/mbpage.htm](http://obssr.od.nih.gov/RFA_PAs/MindBody/mbpage.htm)). These grants terminate in September 2004, and OBSSR intends to expand its efforts, in cooperation with NIH ICs, through a *Mind-Body and Health Research Infrastructure Program*. The primary purposes of the program are to provide resources to support and advance research that will improve the understanding of mind-body interactions and health, facilitate interdisciplinary collaboration among investigators conducting health-related mind-body research, and promote innovative approaches to mind-body and health research questions. An additional goal is to facilitate interaction among scientists in locations throughout the US in order to contribute to the integration and coordination of mind-body and health research. The program will support approximately six center-like grants and four smaller developmental grants, commencing at the close of FY 2004.

**Workshop on Interdisciplinary Training in the Behavioral, Social and Biomedical Sciences.** Numerous committees convened by the National Academy of Sciences (NAS) have concluded that the understanding of behavioral and psychosocial processes is fundamental to understanding disease etiology and to promoting health. Yet, collaboration between social and behavioral scientists and biomedical investigators is relatively uncommon. This may stem, in part, from traditionally trained social and behavioral researchers' lack of expertise in biomedical fields and vice versa. In FY 2002 OBSSR convened a workshop of extramural training grant directors, NAS staff and representatives from numerous ICs to discuss current problems and suggest possible solutions for training investigators to work in interdisciplinary teams to tackle some of our most pressing health problems. OBSSR is currently working with numerous interested ICs to develop *PhD Plus*, a new postdoctoral program that would provide individuals trained in one discipline with formal course work and laboratory training in a second field. A program announcement is anticipated for release in FY 2003, with funding to begin in FY 2004.

***Allostatic Load and the Response to Trauma and Injury.*** Unintentional injury remains the lead cause of death for US citizens under the age of 40. The physiological response to injury is exceedingly complicated. Two seemingly similar individuals with similar injuries often have widely different outcomes, possibly due, at least in part, to the fact that these individuals might actually arrive at the time of injury with very different life-experiences, having encountered a variety of factors which would impact their ability to respond to the injury. Allostatic load has been proposed as a measure of cumulative “wear and tear” on the body, *i.e.*, the price the body pays for having to adapt to various psychosocial challenges and adverse environments. It reflects interactions among genes, development, behavioral choices (e.g., diet, exercise, smoking), social interactions at the family, community and societal levels, and other life experience variables. OBSSR and NIGMS are currently working with an external Planning Committee to explore barriers to and opportunities for research on the topic of allostatic load and the response to trauma and injury. These issues will be explored in depth at an upcoming workshop and will culminate in the issuance of a program announcement in late FY 2003, with funding anticipated to begin in FY 2004.

***Making Behavioral Research More Relevant.*** The health care system is not making optimal use of the recent discoveries in behavioral research. Research on altering harmful behaviors such as tobacco use, unhealthy dietary behaviors, inadequate physical exercise, and risky alcohol use or drug use demonstrates that it is possible to help patients to initiate beneficial behavioral changes. Further research is needed to assist in making these behavioral therapies more practical, applicable to patients with more than one unhealthy behavior, and successful in more diverse patient populations. In order to accomplish this goal, OBSSR is working in partnership with the RWJF, the Agency for Healthcare Research and Quality (AHRQ), and the Centers for Disease Control and Prevention (CDC). In FY 2002, OBSSR and AHRQ funded a University based resource center to work with clinicians to incorporate the latest research findings into their practices and to conduct further research efforts to improve behavioral therapies. CDC and OBSSR are working on improving the information available to clinicians, communities and public health agencies. While applying existing knowledge will be useful both for prevention and treatment, research to identify barriers to current therapies, ways to overcome these barriers, and develop new more effective and versatile approaches is needed.

***Interactions of Work, Family, Health and Well-being.*** Family members often experience conflicts between the demands of work and family life. Foundation and federally funded research has begun to examine the role of family and work on the health and well-being of both families and employees. Scientific evaluation of these workplace

programs will yield useful information about the effectiveness of these programs and about whether these potentially conflicting demands impact family and worker health and well-being. To address this issue, OBSSR is jointly planning a conference for FY 2003 with NICHD, CDC, and the Sloan Foundation. Previous research has examined the relationships between work and health and between family and health, but not the interactions among all three. The goal of the conference is to foster communication between researchers working from these two perspectives, to identify the major gaps in knowledge, to discuss differences in research methods and theoretical approaches, and to foster cross-disciplinary research examining the interaction of paid work, family life, and health. Subsequent conferences in FY 2004 and beyond will address methodological challenges of conducting this type of research and evaluation of existing or new intervention strategies.

*Evaluating Complex Interventions.* Randomized clinical trials have demonstrated the efficacy of a number of behavioral therapies and other types of therapies. Supplemental research strategies are needed to further evaluate how to apply the results of these randomized clinical trials to clinical practice, and to interventions that involve both clinical and community components. Some of this research will involve randomized trials in clinical settings or community settings but some may involve other research designs. This research has often been labeled as either effectiveness research or as research on defined populations. This research may involve systems level changes in health care systems. It may involve dissemination of information to clinicians, patients, and communities. The optimal research designs for this type of research need further exploration and the development of evaluation criteria for this type of research also need further development. In FY 2003, OBSSR working with NIH ICs and CDC proposes to organize a workshop addressing both the design and the evaluation of this research.

## The Office of Dietary Supplements

### Introduction

The Office of Dietary Supplements (ODS) was established in 1995 under the Dietary Supplement Health and Education Act (DSHEA). In 1998, ODS released its Strategic Plan, available on the ODS website (<http://ods.od.nih.gov>). The plan identified five scientific goals: (1) to evaluate the role of dietary supplements in the prevention of disease and reduction of risk factors associated with disease; (2) to evaluate the role of dietary supplements in physical and mental health and in performance; (3) to explore the biochemical and cellular effects of dietary supplements on biological systems and their physiological impact across the lifespan; (4) to improve scientific methodology as related to the study of dietary supplements; and (5) to inform and educate scientists, health care providers, and the public about the benefits and risks of dietary supplements. The budget request for ODS to meet these goals for FY 2004 is \$18.778 million.

### Science Advances

ODS has made significant progress toward meeting its scientific and information strategic goals. Because of substantial increases in the budget for ODS over the last three years, and the opportunities that this has provided for developing new areas of research and education, ODS has embarked on a re-examination of its strategic plan, which will be completed in FY 2003.

### *Scientific Goals*

(i) ODS initiated its *Dietary Supplement Research Centers Initiative* in FY 1999, as a joint effort of 3 NIH units: ODS, National Center for Complementary and Alternative Medicine (NCCAM), and National Institute for Environmental Health Sciences (NIEHS). Two Centers were jointly funded in FY 1999 by ODS and NCCAM at UCLA and University of Illinois at Chicago (UIC) and a third was funded by NIEHS at University of Missouri. Two Centers, jointly funded by ODS and NCCAM, were added in 2000 at University of Arizona and Purdue University. One more Center was funded by ODS and administered by NIEHS in 2002 at Iowa State University. The National Institute of General Medical Sciences and Office of Research on Women's Health (ORWH) have provided additional funding. All Centers, currently focused on botanicals, were funded for an initial period of 5 years. Four of them were designated as P50 Centers (UCLA, UIC, Arizona, Purdue) with budgets of about \$1.5 million per year and two were P01 Program Projects (Missouri, Iowa State) with smaller budgets, about \$1 million per year. In 2001, ODS provided additional funds to the P50 Centers to support further training and career development activities. Training grant requests from the two P01 Program Projects have been submitted and are being considered for funding by ODS. The long-term goal of this program is to meet emerging priorities in dietary supplement research where a multidisciplinary approach is needed. The program will undergo evaluation by external scientific reviewers in FY 2003 as a prelude to releasing an RFA for re-competition of the program in FY 2004.

(ii) ODS has published the proceedings of conferences that it sponsored in FY 2001 and 2002:

*Dietary Supplement Use in Children*, a conference organized by the National Institute of Child Health and Human Development (NICHD) and ODS; proceedings were published in summary form (Raiten DJ, Picciano MF, Coates PM: Dietary supplement use in children: who, what, why, and where do we go from here? Executive summary. *Nutrition Today* 37: 118-120, 2002 and 167-169, 2002). This conference is the first in a series devoted to supplement use across the lifespan. A second was held on the topic of *Dietary Supplement Use in Women of Reproductive Age*, jointly organized by ODS, NICHD, and ORWH in early 2002. A third, on *Dietary Supplement Use in the Elderly*, was held in early 2003, jointly organized by ODS and the National Institute on Aging (NIA). A National Library of Medicine Bibliography of Research on Dietary Supplements in the Elderly was a companion piece to the conference; it will be available on the web for consumers and researchers, and will be updated yearly.

*The Science and Policy of Performance-Enhancing Products*, organized by ODS in partnership with the Council for Responsible Nutrition; proceedings were published in

summary form with a set of research recommendations that emerged from the conference

(Fomous CM, Costello RB, Coates PM: Symposium: conference on the science and policy of performance-enhancing products. *Medicine and Science in Sports and Exercise* 34: 1685-1690, 2002).

*Diet, DNA Methylation Processes, and Health*, organized by the National Cancer Institute (NCI), ODS, and others; proceedings were published as a supplement to the *Journal of Nutrition* 132 No. 8S (August, 2002). This conference led to the release of two research initiatives, a Program Announcement (PA) and a Request for Applications (RFA), jointly sponsored by NCI and ODS in FY 2002. It also led directly to another conference, co-sponsored by NCI and ODS as well as NCCAM, on Nutrigenomics and Proteomics held in FY 2002.

Several other co-sponsored workshops from FY 2002 are being prepared for publication.

(iii) In FY 2000, ODS sponsored a workshop on the role of chromium in the prevention and treatment of Type 2 diabetes mellitus. This workshop was designed to develop a research agenda for basic and clinical investigation of chromium in this disease. As a result of the workshop, ODS commissioned a systematic review of the clinical trials literature relating chromium supplementation to the prevention and treatment of diabetes; it was published in 2002 (Althuis MD, Jordan NE, Ludington EA, Wittes JT: Glucose and insulin responses to dietary chromium supplements: a meta-analysis. *American Journal of Clinical Nutrition* 76: 148-155, 2002). It led to release of a PA in collaboration with the National Center for Complementary and Alternative Medicine (NCCAM) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). ODS has funded or co-funded several grants received in response to the PA.

(iv) In FY 2001, ODS co-sponsored a workshop with the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and NCCAM on the role of s-adenosylmethionine (SAdMe) in liver disease. Papers from that conference were published in the journal *Alcohol* 27 No. 3 (July 2002). An RFA was released in FY 2002; ODS co-funded several grants with NIAAA and NCCAM resulting from that RFA.

(v) ODS continues to support investigator-initiated research in partnership with other Institutes and Centers at NIH. In FY 2002, ODS expanded its portfolio of co-funded grants; we now collaborate with 14 Institutes and Centers in funding 51 grants. They include topics such as basic studies of metabolism of dietary supplement ingredients, methods for botanical supplement analysis, in vitro and in vivo pre-clinical studies, and clinical trials of dietary supplements. ODS will continue to stimulate research through conduct of conferences, workshops, and presentations at national and international meetings. ODS will continue to promote new research initiatives through co-funding of conferences proposed by the other Institutes and Centers at NIH. In FY 2002, ODS co-sponsored 18 conferences and workshops on a wide range of topics relevant to dietary supplement research.

(vi) To enhance understanding of the safety of dietary supplements, ODS will continue to partner with the Office of the Secretary of Health and Human Services to support the efforts of the Dietary Reference Intakes (DRI) panels relevant to dietary supplements. These panels operate under the auspices of the Food and Nutrition Board of the Institute of Medicine.

### *Information and Education Goals*

(i) The *International Bibliographic Information on Dietary Supplements* (IBIDS) database was launched in FY 1999, and continues to receive a very high volume of web traffic. It contains reference to more than 600,000 papers in the international scientific literature on dietary supplements. The project is jointly organized by ODS and the National Agricultural Library of the US Department of Agriculture (USDA). ODS expanded the service on this website in

FY 2001 to include a consumer-oriented version that provides the ability to search just the consumer-oriented literature contained in IBIDS. ODS seeks to add unique citations not captured by other publicly available databases with literature on dietary supplements. The database is updated quarterly.

(ii) The second database, *Computer Access to Research on Dietary Supplements* (CARDS), was released early in FY 2002. It is a resource for academic, government, private sector, and other audiences interested in the array of research studies in dietary supplements that are funded by the federal government. The initial release of CARDS in FY 2002 contained data on NIH-funded research for FY 1999, the first year in which Institutes and Centers at NIH began reporting data on research funding in the area of dietary supplements. In early FY 2003, NIH data for FY 2000 and FY 2001 were added and work is proceeding to include data from other federal agencies.

(iii) ODS and the NIH Clinical Center have completed the first collection of Fact Sheets about specific vitamin and mineral dietary supplements for dissemination in print and on the Internet through our website (<http://dietary-supplements.info.nih.gov>). These are regularly reviewed for timeliness and accuracy. Additional Fact Sheets are planned for this series.

(iv) ODS collaborates with NCCAM to develop a series of Fact Sheets on botanical dietary supplements. The Fact Sheet on black cohosh was posted on the ODS web site in October 2002. Fact Sheets on valerian and kava, as well as one containing background information on botanicals are nearing completion.

(v) ODS collaborates with NCI to provide scientific oversight and support for developing the dietary supplement component of a nutrition teaching tool for first-year medical students with subsequent development for nurses and pharmacists. A valuable new component of this tool is one on athletic performance enhancement with dietary supplements. As dietary supplement information is increasingly recognized as an important part of nutrition education, ODS will explore other opportunities to contribute

to undergraduate, graduate, and medical school education programs that feature dietary supplements.

(vi) ODS has made several presentations about NIH funding strategies, ODS programs, and current issues in dietary supplement use to a wide variety of audiences. These include: professional academic society audiences (e.g., American Dietetic Association, Society for Nutrition Education, American Society for Nutritional Sciences, Association of Pharmaceutical Scientists, American Society of Pharmacognosy, American Association of Cereal Chemists); industry-sponsored meetings (e.g., Nutracon, Council for Responsible Nutrition, National Nutritional Foods Association, Consumer Health Products Association, American Herbal Products Association); and meetings sponsored by other non-governmental organizations (e.g., Life Sciences Research Office, International Food Information Council, Food and Drug Law Institute, International Life Sciences Institute). These efforts provide up-to-date information about research activities and opportunities for academic and industry-based investigators to compete for NIH funds in dietary supplement research. ODS staff have provided similar information at international meetings, since government and private sector organizations around the world are interested in how the NIH, and particularly ODS, supports research.

### **New Initiatives**

#### ***Evidence-based Reviews of Dietary Supplement Efficacy and Safety***

ODS conducts detailed reviews of the efficacy and safety of dietary supplement ingredients, in consultation with NCCAM, the Food and Drug Administration (FDA), and the Agency for Healthcare Research and Quality (AHRQ). ODS coordinates the development of an evidence-based research agenda with a broadly-based government group and employs AHRQ's Evidence-Based Practice Center (EPC) program to conduct these reviews.

The first review, on ephedra in weight management and athletic performance, will not only provide detailed information about the state of the science about this ingredient, but will also measurably assist us in developing future research activities to address both the efficacy and safety of products containing ephedra. The report, being conducted by the RAND-Southern California EPC, will be completed in early 2003.

Senate Report language accompanying the FY 2002 budget appropriation for NIH called for the systematic review of literature related to the health benefits of omega-3 fatty acids, particularly with respect to heart disease. ODS has worked closely with the National Heart, Lung, and Blood Institute (NHLBI), as well as with other Institutes and Centers, to develop the task order for this review. Three EPCs (RAND-Southern California, University of Ottawa, and New England Medical Center) are collaborating to produce a series of nine reports on the effects of omega-3 fatty acids on a number of body systems/conditions including cardiovascular disease, infant growth and development, and mental disorders. As the completed reports become available over the next two years, ODS will work with NIH Institutes and Centers to develop appropriate research agendas.

**ODS is currently evaluating a variety of topics for additional evidence-based review. Topics will be prioritized based on their potential as feasible research agendas, and several of them will be initiated in FY 2003.**

#### ***Ephedra Research Agenda***

**Congressional report language accompanying the FY 2001 budget asked ODS to develop a research program related to botanical supplements that contain ephedra; Senate enthusiasm for this program was further noted in report language for FY 2002 and FY 2003. As noted above, we have commissioned an evidence-based review of ephedra efficacy and safety. The report is being done by RAND, and will be completed in early 2003. It will provide the basis for discussions by a working group of experts being convened by ODS and NCCAM to provide NIH with options for future research on the efficacy and safety of ephedra. ODS nominated ephedra for study by the National Toxicology Program (NTP) of NIEHS, and protocols for its study in relevant animal models are currently being evaluated.**

#### ***Support for National Surveys of Dietary Supplement Use***

**ODS continues to support the National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics at the Centers for Disease Control and Prevention (CDC), for those aspects of the survey concentrating on dietary supplement use in the US population. This will inform future research about dietary supplement use in important target populations, such as children, women, and the elderly. Funding is used to create and populate a database of dietary supplements to assist with the survey, as well as to support the measurement of blood levels of key metabolites associated with dietary supplement use.**

**In FY 2002, ODS co-sponsored a workshop with USDA to examine the emerging needs for dietary assessment, including supplement use, in national surveys such as NHANES. One result will be a publication of the major issues discussed at the conference. Another key outcome has been to develop a database of dietary supplement ingredients that is analytically based and that can ultimately be used to support federally-funded studies such as NHANES, as well as other investigations of dietary supplement use.**

#### ***Dietary Supplement Analytical Methods and Reference Materials Program***

**Senate report language accompanying the FY 2002 appropriation (and reiterated in the Senate report for FY 2003) called on ODS to establish a program to develop, validate, and disseminate analytical methods and reference materials, primarily but not exclusively for botanical supplement ingredients. ODS created a new program to handle this challenge; the program has already begun to coordinate these activities among government agencies, non-government organizations, academia, and the private sector. ODS funds a major activity in analytical method validation by the Association of Official Analytical Chemists (AOAC) International, in collaboration with the Food and Drug Administration (FDA).**

ODS collaborates with the National Institute of Standards and Technology (NIST) to develop standard reference materials for dietary supplements; FDA is a partner in this activity. Both of these programs will be expanded in future years through the use of targeted initiatives for development and validation of methods and standards.

### *Training and Career Development*

ODS is committed to expanding the career opportunities for investigators in dietary supplement research. Strategies already in place and under further development include: travel support for young investigators to attend and present data at scientific meetings in the field of dietary supplements; establishing with other Institutes and Centers at NIH the co-funding of Fellowship (F-series) and Career Development (K-series) awards to young investigators with a desire to train in this area; and funding the research career development of selected NIH intramural fellows. Supplementary support to the Dietary Supplement Research Centers was provided in FY 2002 to encourage training of graduate students and postdoctoral fellows at these centers of excellence; this support will continue for the duration of the grants.

### *Expansion of Efforts to Partner with Industry to Advance Research Goals*

ODS is committed to developing opportunities with the private sector to enhance research efforts in the area of dietary supplements. To this end, ODS will explore opportunities for co-sponsoring conferences and workshops. A colloquium with industry to explore areas of mutual research interest was held by NCCAM with ODS collaboration in May 2001. ODS co-funded 3 Small Business Innovation Research (SBIR) grants during FY 2002 and will continue to collaborate with other NIH Institutes and Centers in this program. ODS partnered with the Council for Responsible Nutrition to convene a conference on the Science and Policy of Performance Enhancing Products early in 2002. ODS will use the outcome of this conference to help it and other NIH partners to develop an appropriate research agenda in this area. ODS is regularly present at meetings of industry groups to provide information about NIH programs that may be of interest to them. ODS has a joint project, now in its third year, with the Consumer Health Products Association to publish an Annual Bibliography of Significant Advances in Dietary Supplement Research.

### Other Areas of Interest

#### *National Nutrition Summit*

The National Nutrition Summit was held in May 2000 in Washington, DC. This major national meeting was organized jointly by the Department of Health and Human Services (DHHS) and the USDA, with ODS leading the DHHS component of this effort. Follow-up activities of the Summit included convening a Surgeon-General's Listening Session on Overweight and Obesity in December 2000, publication of portions of the Summit in various journals, and presentations at meetings. Constituencies participating in the Summit have begun to develop public-private partnerships around issues and concerns (such as overweight/obesity and hunger) that were raised at the Summit. A paper has been

submitted to the Journal of Nutrition that provides an overview of the history, purpose, and overarching themes of the Summit. A second paper summarizing the highlights of the Summit will be published in Nutrition Today. ODS has taken the lead in developing a permanent website to feature the activities of the Summit and its follow-up initiatives. The website is now available at <http://www.nns.nih.gov>.

### *International Activities*

Micronutrient deficiencies remain a problem in many parts of the world. The ODS partners with other NIH Institutes and Centers, such as the Fogarty International Center (FIC), as well as other organizations within and outside the federal government, to improve the quality of research needed to implement effective micronutrient assistance programs in diverse settings around the world. Part of this initiative has been to co-fund grants with FIC to promote research by US-trained foreign scientists who have returned to their countries of origin. Another international effort that is co-sponsored by several NIH units, including ODS, is entitled Brain Disorders in the Developing World: Research Across the Lifespan.

## **The Office of Rare Diseases**

### **Introduction**

The Office of Rare Diseases (ORD) supports activities that stimulate, coordinate, and support research on rare diseases and conditions. A rare or orphan disease is defined as a disease, illness, syndrome, or condition affecting fewer than 200,000 Americans.<sup>1</sup> Although the prevalence of each disease may be quite small, more than 20 million Americans are estimated to suffer from the more than 6,000 known rare diseases.<sup>2 3</sup>

On November 6, 2002, President Bush signed into law P. L. 107-280, the Rare Diseases Act of 2002. The law formally establishes the ORD and authorizes an increase in the national investment in the development of treatments for patients with rare diseases.

The budget request for the ORD is \$11.423 million, an increase of \$.224 million above the FY 2003 level.

### **Science Advances**

In FY 2002, the ORD co-funded 59 national and international scientific workshops in collaboration with NIH Institutes and Centers and other organizations. ORD co-funds these workshops when a particular scientific opportunity exists or if little or no research is underway for a particular rare disease or disease group. Findings from an evaluation of the workshops

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<sup>1</sup> The definition of a rare disease is in the Orphan Drug Act of 1983

<sup>2</sup> The Committee Report on the Rare Diseases Act of 2001, dated December 12, 2001, page 2

<sup>3</sup> As shown in the Rare Diseases List on the ORD website at <http://ord.aspensys.com/diseases.as>

indicate that this program is an effective means in generating research ideas and subsequent grant applications, especially for multicenter trials in rare disease areas that otherwise might not attract much attention.

Examples of workshops focused on specific rare diseases include:

Alpha1- antitrypsin deficiency

Familial dysautonomia

Lowe syndrome

Lymphomatoid granulomatosis

Mucopolysaccharidoses

Multiple hereditary exostoses

Oxalosis

Progressive multifocal leukoencephalopathy

Tuberous sclerosis complex

In addition to the scientific workshops, ORD will also support a series of regional meetings during FY 2003. One of the major goals of these regional workshops is to discuss with patient support groups all aspects of research and research opportunities in NIH's extramural and intramural research programs.

FY 2004, the ORD is planning to fund 75 scientific workshops with a special emphasis of the increase on rare diseases where little or no research exists.

### **New Initiatives**

In FY 2002, ORD in collaboration with the NIH Institutes and Centers leveraged its research funds by supporting 42 rare disease supplemental research grants. The research grants will support research on more than 70 rare diseases including various epilepsies, scleroderma, neonatal lupus, bipolar disorder in preschool children, Joubert syndrome, fetal stroke, Sturge-Weber syndrome, Alagille syndrome, Smith-Lemli-Opitz syndrome, hemophilia, gastrointestinal stromal tumor, childhood-onset schizophrenia, and fetal alcohol syndrome.

ORD provided support in FY 2002 to seven planning grants in anticipation of the publication of a Request for Applications for Rare Diseases Research Centers in FY 2003. The planning grants address the following rare diseases groups: Disorders of peroxisome functions and peroxisome biogenesis; inherited disorders of mitochondrial metabolism; inborn errors of urea synthesis; lysosomal storage disorders; epigenetic and genetic rare disorders; developmental degenerative disorders of the cerebellum; and central nervous system (CNS) developmental disorders.

ORD also provided support for the biliary atresia research centers in collaboration with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

In FY 2003, the ORD will establish and support seven centers for clinical research into, training in, and demonstration of diagnostic, prevention, control, and treatment methods for rare diseases. The rare diseases research centers will each encompass a number of locations across

the U.S., and will be multidisciplinary, involving a network of experienced investigators in complementing areas of expertise. In addition to the increased focus on the particular rare diseases group, the benefit of each center will include a better integration of the research activities of various disciplines than would be possible if each research project were pursued individually, and, in some cases, an existing framework that provides optimal settings for medical investigators to conduct safe, controlled, inpatient and outpatient studies of both children and adults. Also, the distribution of research locations across the U.S. will make investigational treatments more accessible to patients with rare diseases.

To complement these extramural centers, the ORD will develop in collaboration with NIH Institutes and Centers a rare diseases intramural research program. One component will be for patients with rare illnesses where a diagnosis has been elusive despite previous extensive efforts to determine the exact nature of the medical problem. The program will address specific rare diseases research including the natural history, development of specific experimental diagnostic tests of rare diseases, validation of the tests, and clinical pilot studies. The intramural research efforts will benefit from the availability of an existing corps of NIH-based biomedical and genetic research experts. The rare diseases intramural research program will also provide support for training programs in biochemical genetics and in clinical research..

Another component of the ORD intramural research program will be a collaboration with several NIH Institutes to fund at least five Bench to Bedside Grants that focus on rare diseases. These grants promote joint research projects among NIH-based clinical, translational, and basic scientists to affect the translation of findings from the laboratory to clinical applications.

Research on rare diseases is often hampered by difficulty in locating enough patients with a particular disorder. To address this difficulty, ORD is considering the development of a Health Information Patient Privacy Act (HIPPA)-compliant rare diseases patient registry. By facilitating the matching of researchers and geographically widespread research subjects by a reliable third-party organization, the registry will assist research on rare diseases without compromising the privacy of potential research subjects. Such a registry is essential to accelerated basic and epidemiologic research on rare diseases as well as clinical studies on new methods for treatment and prevention.

In FY 2004, the ORD will continue its support of the rare diseases intramural and extramural research programs.

### **Other Areas of Interest**

In FY 2004, the ORD will continue to co-fund with the National Human Genome Research Institute the Genetic and Rare Diseases Information Center. The information center provides free-of-charge understandable and valid information to patients and their families, health professionals, researchers, and to the public. Also, ORD will support an additional focus on making the information center more accessible to minority and under-served populations.

### **Science Education Activities**

## **Introduction**

The Office of Science Policy (OSP), through its Office of Science Education (OSE), serves as an educational liaison between the National Institutes of Health (NIH) and the nation's public. The OSE coordinates science education activities at the NIH and develops model science education programs, which serve diverse populations including under-served communities, women and minorities. The mission of the OSE is to help people understand and use new knowledge uncovered by the NIH in pursuit of better health for everyone. The OSE works toward this mission by: creating programs to improve science education in schools; creating programs to advance public understanding of medical science, research and careers; promoting NIH educational resources and programs; and advising NIH leadership about science education issues.

## **Current Activities & New Initiatives**

The OSE's programs target different sectors of the public: school systems -including teachers, school administrators, and students; and the general public. Certain programs serve overlapping target audiences.

The OSE's most important activity is the development and distribution of The NIH Curriculum Supplements. These National Science Education Standards-based K-12 supplements are free, ready-to-use, interactive teaching units that result from the unique partnering of NIH scientists, teachers, and expert curriculum developers. They incorporate the best of both science and education communities, and are intended to introduce new concepts and supplement materials that are out-dated.

To date, over 100,000 copies of the NIH curriculum supplements have been distributed to science teachers, college professors and home-schoolers.

The office continues to develop, field test, refine, disseminate, and evaluate new supplements each year. In collaboration with different NIH IC's, and the highly respected curriculum developer Biological Sciences Curriculum Study (BSCS), OSE has plans for 15 different curriculum supplements that are in various stages of development. By FY 2004, the office expects to be distributing 6 high school units, 5 middle school units, and 1 elementary school unit. Hard copies of these materials will continue to be distributed to teachers and home-schoolers. In addition, web versions of the first twelve supplements will be available to anyone wishing to use them. OSE is modifying the existing supplements to meet Section 508 accessibility standards for web publication. During FY 2004 two new middle school units (one, on the process of scientific inquiry, and the second, on musculoskeletal and skin diseases) will undergo national field-tests. Results from OSE's evaluations, conducted in collaboration with the National Science Foundation, will be used to refine the development of new supplements.

In partnership with the Office of Research on Women's Health (ORWH), the Office has developed two programs encouraging middle-school girls to consider careers in science. During this critical time in their lives, students make decisions about academic courses that

may affect their career options. The first, Women are Scientists Video and Poster Series, consists of colorful, informative video and poster sets that depict successful women scientists as inspirational role models. Three sets are currently available, and a fourth featuring women scientists with disabilities is being developed in FY 2003 and FY 2004. Plans for the series also include having the videos online. The second program is the Women in Science Poster Series. This is a series of posters with a companion web site that emphasizes that medical research offers many different career paths, all of which are open to women. Three posters have been produced and two more will begin development in FY 2003. In both programs, the racial and ethnic diversities of the women depicted help to make the posters relevant to a large number of girls, in particular, those from populations currently under-represented in scientific and medical careers.

The NIH Speakers Bureau is comprised of research scientists, clinicians, and other NIH professionals who speak on a variety of health, medical and science research topics, and related careers to local schools and other community groups. These speaker's will serve as real career examples to be cross-referenced with OSE's new career web site, LifeWorks (launched in FY 2003).

In FY 2004, the OSE will continue to facilitate several of its popular public education programs. One program is the NIH Mini-Med School, a free public science education lecture series that is held once a week in the spring for 10 consecutive weeks. There are 500 Mini-med students who attend and study the same subjects that real first and second-year medical students do. The lectures are presented by experts in the field and cover topics, which graduate over the sessions from the basic sciences to broad medical science themes. Another public education program is Science in the Cinema, a free film and discussion series held in the summer for 6 consecutive weeks. Each week a film with a medical science theme is screened. Immediately following, an expert in the film's subject area will lead an audience discussion about the science depicted in the film. Program participants have grown from less than 200 to as many as 1300 people since it began in 1994.

In FY 2003, in partnership with the US Department of Labor, the OSE launched a new web-based public science education program that focuses on careers in science and health, called LifeWorks. This in-depth career database allows students to explore a broad range of career options, and details the knowledge, skills, abilities, education and experience required for a given career. Non-science careers that support the NIH mission, such as Medical Illustrators, Program Managers, Library Curators, and Patent Attorneys will also be added.

### **Other Areas of Interest**

To maximize the effectiveness of the NIH curriculum supplements on science achievement nationwide, OSE continues to emphasize professional development programs for teachers. The office will pursue partnerships with NIH-sponsored research centers, universities, professional societies, and science education organizations. Through these partnerships,

**OSE will "train the trainers" on the proper implementation of the NIH Curriculum Supplements, who can in-turn train other teachers.**

**In FY 2002, the OSE formed the Diversity Work Group (DWG) - a team dedicated to increasing the participation of minority and under-served populations in all of OSE's programs. The DWG has identified numerous organizations and media contacts that serve these populations, through which OSE can promote it's educational programs. The group's first initiative was successful - a marked increased in**

**the enrollment of minorities in the Spring 2002, Mini-Med School program. The DWG has also developed a list of activities, approved by the OSE Director that will span the next two years.**

**The budget request for OSE in FY 2004 is \$3.866 million.**

### **Loan Repayment and Scholarship Programs**

#### **Science Advances**

**In FY 2002, through the loan repayment and scholarship programs authorized under the NIH**

**Revitalization Act of 1993, the NIH Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds (CR-LRP) awarded a total of twelve (12) two-year contracts and eleven (11) one-year renewal contracts at a cost of \$1.136 million. The awardees agreed to conduct clinical research as NIH employees during their contract period, while the NIH agreed to provide up to \$35,000 repayment per year toward their educational debt. In addition to educational loan repayments, the CR-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as additional State and local taxes, as compensation for the increased tax burdens resulting from the receipt of loan repayments. For FY 2003, the CR-LRP plans to award contracts to (15) fifteen individuals entering into initial two-year contracts, and fourteen (14) contracts to individuals entering into one-year renewal contracts at a cost of \$1.278 million.**

**In FY 2002 the NIH awarded \$3.184 million to fifty-six (56) individuals under the Loan Repayment Program for Research Generally (GR-LRP). Awards were made to fund forty-eight**

**(48) initial three-year contracts and eight (8) one-year renewal contracts to participants who are**

**physicians or scientists engaged in either basic or clinical research activities at the NIH.**

**This**

**program is intended to recruit and retain health professionals to non-trainee NIH intramural**

**positions; thus, such individuals will generally be considered for permanent and/or tenure-track positions. GR-LRP participants agree to a minimum service contract period of three years. In addition to educational loan repayments of up to \$35,000 per year, the GR-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as**

additional State and local taxes, as compensation for the increased tax burdens resulting from the receipt of loan repayments. For FY 2003, the GR-LRP plans to award contracts to fifty (50) individuals entering into initial three-year contracts, and eleven (11) contracts to individuals entering into one-year renewal contracts at a cost of \$3.345 million.

The NIH continued to support the Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds (UGSP). In FY 2002, scholarship awards and funding for service pay-back were provided in the amount of \$.892 million to eighteen (18) undergraduate students and thirteen (13) graduate students who agreed to pursue academic programs appropriate to support positions required by NIH's intramural research and training programs. In satisfaction of statutorily mandated service requirements, scholars agreed to employment at the NIH for one year for each year of scholarship support after graduation, with deferment of the service requirement possible for those who pursue appropriate graduate and medical school training, and for ten weeks during the academic year. For FY 2003, the UGSP plans to award scholarships and provide funding for summer internship service pay-back for twenty-two (22) individuals at a cost of \$ .559 million and provide funding for fourteen (14) individuals performing one-year service pay-back at a cost of \$.462 million.

### **Future Research Directions**

In FY 2004, the budget request is \$6.843 million. The funding will be used for thirty-one (31) awards under the Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds, twenty-one (21) awards for the Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds, and sixty-two (62) awards under the Loan Repayment Program for Research Generally.

### **AIDS Research Loan Repayment Program**

#### **Introduction**

In FY 2002 the NIH awarded \$.712 million to fifteen (10) individuals under the AIDS Research Loan Repayment Program (AIDS-LRP). Awards were made to fifteen (10) health professionals, representing three (3) recipients who entered into one-year renewal contracts and seven (7) researchers who entered into initial two-year contracts. The awardees agreed to conduct AIDS research as NIH employees, while the NIH agreed to provide up to \$35,000 repayment toward their educational debt. In addition to educational loan repayments, the AIDS-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as additional State and local taxes, as compensation for the increased tax burden resulting from the receipt of loan repayments. For FY 2003, the AIDS-LRP plans to award fifteen (15) contracts to individuals entering into initial two-year contracts, and five (5) contracts to individuals entering into one-year renewal contracts at a cost of \$1.5 million.

### **Future Research Directions**

In FY 2004, the OAR request includes \$1.5million for the AIDS LRP. The funding will be used to award contracts to twenty (20) health professionals conducting AIDS research.

### **The Director's Discretionary Fund**

In FY 2004 the NIH Director will continue to maintain a Director's Discretionary Fund (DDF) to allow the Director to respond quickly to new and emerging high priority research opportunities and health priorities.

Given its extensive and complex program portfolio and the need to invest funds productively for the health and defense of the American people, the NIH launched an Agency-wide effort to identify the critical roadblocks and knowledge gaps that constrain rapid advances in biomedical research progress.

The NIH Roadmap is the result of an ongoing series of consultations with scientists charged with thinking broadly about the future. It is comprised of four broad initiatives which will exploit past discoveries to meet tomorrow's challenges: 1) Revolutionary Methods of Research; 2) New Pathways to Discovery; 3) Multi-disciplinary Research Teams of the Future; and 4) Re-engineering the Clinical Research Enterprise.

In the arena of revolutionary methods of research, new and expanded efforts will be undertaken in structural biology, molecular libraries, nanotechnology, and computational biology and bioinformatics. Regarding new pathways to discovery, the NIH will expand and develop programs in systems biology, stem cell research, and behavioral research. The Agency will also work to ensure the nation will have in place the much needed multi-disciplinary research teams of the future. Finally, the NIH will introduce new efforts to re-engineer the clinical research enterprise. The explosion of basic research advances in recent years demands new efforts in clinical research to translate findings from genetics and proteomics into front line treatments. There is a pressing need to rethink the technical and human infrastructure requirements for a more effective clinical research enterprise in this country as a major priority for the upcoming years. A planning effort is underway to identify the major roadblocks and develop potential solutions. The DDF request for FY 2004 is \$45 million of which \$35 million will be used for the NIH Roadmap.

### **Other Areas of Interest**

The FY 2004 estimate also provides \$103.721million for OD Operations. As the NIH has grown over the last several years, the complexity of leading and directing the medical research program has intensified, and the Administration, Congress, and other stakeholders have tasked the NIH OD with myriad new legislative, programmatic, and scientific issues to address and manage. The OD has financed these increased leadership and oversight activities using a combination of its appropriation, the NIH Management Fund, and the NIH Service and Supply Fund. In FY 2002 a task force was established to examine the current funding for programs within the OD and to recommend a standard

**policy for determining what funding source will be used for its activities. The FY 2004 budget request reflects implementation of this policy, and changes the funding source for a number of offices and programs, with many of the changes involving a shift from the NIH Management Fund to the OD appropriation. The FY 2004 OD Operations request provides a level of funding for the OD within its appropriation adequate to ensure effective leadership, direction, and oversight. As part of the OD Operations, several OD offices such as the OER, the Office of Intramural Research (OIR), the OSP, and the Office of Management (OM) provide advice to the NIH Director, policy direction to the NIH research community, and administer centralized support services essential to the daily operation of the NIH. Within the OSP, the Office of Biotechnology Activities (OBA) coordinates the functions of the Recombinant DNA Advisory Committee (RAC); the Secretary's Committee on Genetic Testing (SACGT); and the Secretary's Advisory Committee on Xenotransplantation (SACX).**